

WHAT IS CLAIMED IS:

1                   1.    An array of oligonucleotide probes  
2    for detecting a polymorphism in a target nucleic acid sequence  
3    using Principal Component Analysis, said array comprising at  
4    least one detection block of probes, said detection block  
5    including a first group of probes that are complementary to  
6    said target nucleic acid sequence except that the group of  
7    probes includes all possible monosubstitutions of positions in  
8    said sequence that are within n bases of a base in said  
9    sequence that is complementary to said polymorphism, wherein n  
10   is from 0 to 5, and a second and third group of probes  
11   complementary to marker-specific regions upstream and  
12   downstream of the target nucleic acid sequence, wherein the  
13   third group of probes differs from the second set of probes at  
14   single bases corresponding to known mismatch positions.

1                   2.    The array of claim 1, wherein the polymorphism  
2    is identified as a result of Principal Component Analysis of  
3    hybridization intensities of the array of probes.

1                   3.    The array of claim 1, wherein at least two  
2    alleles of the polymorphism are known.

1                   4.    The array of claim 1, wherein said first group  
2    of probes comprises a plurality of different probes that are  
3    complementary to overlapping portions of said target nucleic  
4    acid sequence.

1                   5.    The array of claim 1, wherein the  
2    monosubstitutions occur at a plurality of distances from a 3'  
3    end of said probes.

1                   6.    The array of claim 1, wherein said detection  
2    block includes between about 8 and 88 different probes.

1                   7.    The array of claim 1, comprising between 1 and  
2    1,000 different detection blocks, each of said detection

3 blocks including probes complementary to different  
4 polymorphisms in said target nucleic acid sequence.

1 8. A method of identifying whether a target  
2 nucleic acid sequence includes a polymorphic variant using  
3 principal component analysis, comprising:  
4 hybridizing said target nucleic acid sequence  
5 to said array comprising at least one detection block of  
6 probes, said detection block including a first group of probes  
7 that are complementary to said target nucleic acid sequence  
8 except that the group of probes includes all possible  
9 monosubstitutions of positions in said sequence that are  
10 within n bases of a base in said sequence that is  
11 complementary to said polymorphism, wherein n is from 0 to 5,  
12 and a second and third group of probes complementary to  
13 marker-specific regions upstream and downstream of the target  
14 nucleic acid sequence, wherein the third group of probes  
15 differs from the second set of probes at single bases  
16 corresponding to known mismatch positions; and  
17 determining hybridization intensities of the target  
18 nucleic acid and the marker-specific regions to identify said  
19 polymorphic variant.

1 9. The method of claim 8, wherein said target  
2 nucleic acid comprises a detectable label.

1 10. The method of claim 9, wherein said detectable  
2 label is a fluorescent group.

1 11. The method of claim 9, wherein said label is a  
2 binding group.

1 12. The method of claim 11, wherein said binding  
2 group is selected from biotin, avidin and streptavidin.

1 13. The method of claim 8, wherein the polymorphism  
2 is identified as a result of Principal Component Analysis of  
3 hybridization intensities of the array of probes.

1           14. The method of claim 8, wherein at least two  
2 alleles of the polymorphism are known.

1           15. The method of claim 8, wherein said step of  
2 determining comprises:

3           a) calculating the control difference between the  
4 average of the hybridization intensities of the second group  
5 of probes, the hybridization intensities comprising control  
6 perfect matches (PM), minus the average of the hybridization  
7 intensities, the hybridization intensities comprising control  
8 single-base mismatches (MM);

9           b) calculating the possible perfect match intensity  
10 and a heteromismatch intensity from the hybridization  
11 intensities for each position of monosubstitutions of the  
12 first group of probes;

13           c) calculating the difference between the possible  
14 perfect match intensity and the heteromismatch intensity for  
15 each position of monosubstitutions of the first group of  
16 probes;

17           d) calculating a normalized difference (ND) by  
18 dividing the difference of step (c) by the control difference;

19           (e) using principal component analysis, identifying  
20 a polymorphism by comparing normalized differences between  
21 individuals in a population.

1           16. The method of claim 15, wherein an ND is calculated  
2 for at least two allele of a polymorphism.

1           17. The method of claim 16, wherein homozygotes and  
2 heterozygotes are detected by combining principal component  
3 analysis for two alleles.